UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/466,698	06/06/95	SANSUNETTI P	2356.0043-02

18N2/0121

FINNEGAN HENDERSON FARABOW
GARRETT & DUNNER
1300 I STREET NW
WASHINGTON DC 20005-3315

EXAMINER	
CAPUTA,A	
ART UNIT	**PAPER NUMBER**
1817	

DATE MAILED: 01/21/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No. 08/466,698	Applicant(s) Sansonetti et al.
	Examiner Anthony C. Caputa	Group Art Unit 1817

☒ Responsive to communication(s) filed on *23 Dec 1997*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-10, 13, and 14* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-10, 13, and 14* is/are rejected.

☒ Claim(s) *1-10* is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Since this application is eligible for the transitional procedure of 37 CFR 1.129(a), and the fee set forth in 37 CFR 1.17(r) has been timely paid, the finality of the previous Office action is hereby withdrawn pursuant to 37 CFR 1.129(a). Applicant's first submission after final filed on 12/23/97 has been entered.

2. Claims 1-10, 13, and 14 are pending.

Claim Rejections - 35 USC § 112/1st paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10, 13, and 14 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the Office Action mailed 4/30/97 (see Paper No. 13).

As set previously, it is apparent that numerous modified Shigella are required to practice the claimed invention.

In the instant case the construction of claimed Shigella mutants requires knowledge of the nucleotide sequence of said genes, which regions are responsible for biological activity, and the number of nucleotides which must be deleted or inserted. Due to the limited teaching of the specification and the unpredictable nature of which mutations are useful one skilled in the art can not practice the invention as claimed absent undue experimentation. In view of the foregoing the only means by which applicants can provide an enabling disclosure for the Shigella mutants is by depositing said mutants and limiting the claims to the deposited mutants.

Applicants urge that the specification provides sufficient teachings for one skilled in the art to practice the claimed invention (see page 5 of applicants' response submitted after final dated October 9, 1997-Paper No. 20). Applicants state that the specification teach of methods of modification to employ in order to inactivate the genes. These arguments are not considered persuasive. The decisional law has held the mere recitation in the specification of a broad concept does not necessarily provide a sufficient basis for broadly claiming it (i.e. transposon mutagenesis). See Ex parte Gardner 157 USPQ 162 (Bd. Pat. Appls and Interf. 1967), In re Cavallilo, 127 USPQ 202 (CCPA 1969). The fact that the terms in a claim are the same as those in the specification does not prevent the claims from being rejected as unduly broad if they define subject matter not define subject matter not described to be the actual invention by means of adequate representative samples. See in re Lund, 153 USPQ 625 (CCPA 1967). In the instant case the construction of claimed Shigella mutants requires knowledge of the nucleotide sequence of genes (i.e. for production and use of iscA, virG, aerobactin, enterochelin), which regions are responsible for biological activity, and the number of nucleotides which must be deleted or inserted. Due to the limited teaching of the specification and the unpredictable nature of which mutations are useful one skilled in the art can not practice the invention as claimed absent undue experimentation.

While it would appear techniques are known in the art for inactivation, as pointed out by applicants (see pages 2 to 4 of applicants' response submitted after final dated October 9, 1997-Paper No. 20) it is **not** routine in the art to screen for positions within the DNA sequence of the gene so that it does not invade the cells, spread within infected cells, or not produce toxins. Because the specification does **not** disclose :

- which regions of the genes are responsible for biological activity;
- the number of nucleotides which must be deleted or inserted;
- the identity of the genes that are responsible for invading cells, not producing toxins, etc.;

-identity of genes that code for use of aerobactin or enterochelin,

-more than one genes would be expected to be involved in toxin production, spreading, and/or invasion;

- no guidance as to which of the essentially infinite possible choices is likely to be successful;

modifications that can be made to inactivate the genes is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986).

Applicants argue Nassif et al. (see Exhibit 1), Baudry et al. (see Exhibit 2), and Maurelli et al (see Exhibit 3) contain the teachings necessary for screening the *Shigella* genes involved in the invasion of cells, spreading within infected cells, etc.. Applicants arguments are not persuasive. Baudry et al. submitted by applicants (see response submitted after final dated October 9, 1997-Paper No. 20-Exhibit 2) sets forth "The available data indicate that the invasive ability of *S flexerni* is a very complex phenomenon which involves many genes and a large array of polypeptides" and "Whether all these gene products are directly involved in the interaction with the cells, or whether a pool of polypeptides is necessary for transformation and/or correct positioning of a unique product is yet not known" (see page 3411, last para) . In view of: 1) the statements of Baudey et al pointed out above; 2) the assay procedures of Nassif et al. are only directed to one gene which encodes for aerobactin; 3) case law sets forth the general process of isolating DNA does not mean that the claimed specific compound was precisely envisioned or obvious (see *In re Deuel* 34 USPQ2d 1210 Fed Cir 1995) and; 4) modifications that can be made to inactivate the genes are unpredictable as set forth above the rejection under 35 U.S.C. § 112, first paragraph, for lack of enablement is maintained.

Beyond the reasons set forth above, applicants arguments are not sufficient to obviate the rejection in view of *Fliers v. Sugano,* 25 USPQ 2d 1601 (Fed. Cir. 1993) and *Amgen Inc. v.*

Chugai Pharmaceutical Co., Ltd., and Genetics Institute., Inc., 18 USPQ 2d 1016 (Fed. Cir. 1991) as set forth in the prior Advisory Action mailed 9/26/97.

Double Patenting

4. The prior provisional rejection of claim 13 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over copending application Serial No. 08/118,100 is maintained for the reasons of record.

Applicants requested to hold this rejection in abeyance until allowable subject matter has been indicated in either case. The Examiner notes that USSN 08/118,100 has been allowed. Until applicants submit a proper terminal disclaimer said rejection is maintained.

Claim Objections

5. **(NEW)** Claim 1-~~12~~ 10 are objected to because of the following informalities:

Claim 1 and dependent claims are objected for use of the phrase "uninfected, cells". Appropriate correction is required.

Claim Rejections - 35 USC § 112 2nd paragraph

6. **(NEW GROUNDS OF REJECTION)** Claims 2-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4 and 7 are vague and indefinite for use of the phrase "intra-intercellular spread". Do applicants intend to claim intracellular and intercellular spread?

Claim 8 is vague and indefinite for use of the phrase "the first gene comprises the ...genes" since a gene (e.g. the first gene) is comprised of a single gene (i.e. ent F gene) and not more than one gene as recited.

Claim 10 is rejected for being vague and indefinite since it is not clear what constitutes as "in vitro mutagenized genes" . Do applicants intend to claim genes which are mutagenized in vitro? Beyond this claim 10 is vague and indefinite since is not clear if applicants intend to claim "in vitro mutagenized genes" which have the properties of 1) "significant portions have been deleted and 2) marker genes inserted. Finally claim 10 is vague and indefinite since is not clear what constitutes as "significant portions".

Claim 2 and dependent claims thereof rejected since it is not clear what is "wholly or partly removed or permanently inactivated" For instance, do applicants intend the first or second gene be wholly or partly removed or permanently inactivated? Finally claim 2 is rejected for being vague and indefinite for use of the phrase "wholly or partly removed or permanently inactivated" since a gene which is wholly removed is permanently inactivated.

Claim Rejections - 35 USC § 112/4th paragraph

7. **(NEW GROUNDS OF REJECTION)** Claim 9 is rejected under 35 U.S.C. § 112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Claim 9 is rejected since the term "mutagenized" does not further limit the subject matter of the previous claim (e.g. claim 5). A modification of first, second and third gene as recited in claim 5 is mutagenized as recited in dependent claim 9

Specification

8. The disclosure is objected to because of the following informalities:

The instant application does not contain specific reference to the status of the prior application(s) in the first sentence of the specification.

9. Any inquiry concerning this communication should be directed to Dr. Anthony C. Caputa, whose telephone number is 703-308-3995. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is 703-308-0196.

Papers related to this application may be submitted to Group 1817 by facsimile transmission. Papers should be faxed to Group 1817 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the official Gazette 1096 OG 30 (November 15, 1989). The CMI Fax Center number is (703)-308-4242.

Anthony C. Caputa, Ph.D.
January 18, 1998

ANTHONY C. CAPUTA
PRIMARY EXAMINER
GROUP 1800